

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference HAR/001 PCT	<b>FOR FURTHER ACTION</b> see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/IL04/00759	International filing date ( <i>day/month/year</i> ) 19 August 2004 (19.08.2004)	(Earliest) Priority Date ( <i>day/month/year</i> ) 19 August 2003 (19.08.2003)
Applicant AGOS BIOTECG LTD.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 6 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the Report**

- a. With regard to the **language**, the international search was carried out on the basis of:
- ☒ the international application in the language in which it was filed.
- ☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))
- b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 Rule 43.6 *bis(a)*
- c. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.
2. ☐ **Certain claims were found unsearchable** (See Box No. II)
3. ☒ **Unity of invention is lacking** (See Box No. III)
4. With regard to the **title**,
- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

- a. the figure of the **drawings** to be published with the abstract is Figure No. \_\_\_\_\_
- ☐ as suggested by the applicant.
- ☐ as selected by this Authority, because the applicant failed to suggest a figure.
- ☐ as selected by this Authority, because this figure better characterizes the invention.
- b. ☒ none of the figures is to be published with the abstract.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/IL04/00759

## Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of:

a. type of material

☒

a sequence listing

☐

table(s) related to the sequence listing

b. format of material

☒

on paper

☒

in electronic form

c. time of filing/furnishing

☒

contained in the international application as filed

☒

filed together with the international application in electronic form

☐

furnished subsequently to this Authority for the purposes of search

2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/IL04/00759

## Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-4,6,8-18,20,22-26,28-32,35 and 36

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/IL04/00759

## A. CLASSIFICATION OF SUBJECT MATTER

IPC: **C07K 14/00**( 2006.01);**C07H 21/04**( 2006.01);**C12N 15/00**( 2006.01);**A61K 38/00**( 2006.01)

USPC: 530/350;536/23.5;435/69.1;514/2

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 530/350;536/23.5;435/69.1;514/2

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Continuation Sheet

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BUONANNO et al., Neuregulin and ErbB Receptor Signaling Pathways in the Nervous System. Curr. Opin. Neurobiol., June 2001, Vol 11, No. 3, pages 287-296.	1-4, 6, 8-18, 20, 22-26, 28-32, 35 and 36

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

11 June 2008 (11.06.2008)

Date of mailing of the international search report

16 JUL 2008

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

Facsimile No. (571) 273-3201

Authorized officer

Xiaozhen Xie, Ph. D.

Telephone No: 571-272-1600

**BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING**

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1-26, 28-32, 35, 36, drawn to a polypeptide and a pharmaceutical composition thereof comprising a splice variant of an ErbB ligand, an isolated polynucleotide and a vector encoding same, a host cell comprising the polynucleotide, and a method of treating a disease related to an ErbB receptor comprising administering the polypeptide.

Group II, claims 27, 34, drawn to an antisense oligonucleotide, and a pharmaceutical composition thereof.

Group III, claims 33, 37, 38, drawn to gene therapy.

Group IV, claims 39, 40, drawn to a method for selectively enhancing the proliferation or differentiation of stem cells which express ErbB receptors, comprising exposing the cells to an ErbB ligand splice variant.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

A: A polypeptide having the sequence set forth in any one of: SEQ ID NOs: 73-84, 93, 95-104, 109-121

The following claims are generic: 1, 32, 15, 27, 34, 35 and 39.

B: A polynucleotide having the sequence set forth in: SEQ ID NOs: 128-139, 148-165-182

The following claims are generic: 15, 33 and 37.

The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The first inventive concept is the first appearing product, and a method of making it, and a method of using it, set forth for Group I for SEQ ID NO: 73. The remaining products do not share a special technical feature because they differ structurally and functionally. PCT Rules provide for the examination of the 1<sup>st</sup> claimed product, the 1<sup>st</sup> claimed method of making that product, and the 1<sup>st</sup> claimed method of using that product in one application. However, the PCT rules do not provide for the examination of multiple products, multiple methods of making one product, or multiple methods of using one product in one application.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

Groups I includes several different polypeptides that lack a special technical feature because they have different sequences. The amino acid sequence of SEQ ID NO: 73 represents an independent inventive concept from SEQ ID NOs: 74-84, 93, 95-104 and 109-121 because the sequence of SEQ ID NO: 73 is distinct from the other sequences. SEQ ID NO: 73 is considered to be part of the first inventive concept. Each of SEQ ID NOs: 74-84, 93, 95-104 and 109-121 are considered to be additional inventions. Likewise, Groups II-IV embrace multiple independent polypeptides, antisense oligonucleotides, and so forth.

The first inventive concept is considered to be a polypeptide having the sequence of SEQ ID NO: 73, and a method of making it, a method of using it. The claims as written embrace multiple methods and products and will be considered to the degree that they reflect this first invention and any additional inventions paid for. If no additional fees are paid, the first invention in claims 1-26, 28-32, 35 and 36 will be searched and examined with respect to the polypeptide having the sequence of SEQ ID NO: 73.

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/IL04/00759

Continuation of B. FIELDS SEARCHED Item 3:

EAST: USPAT, US-PGPUB, DERWENT, EPO, JPO

STN: Medline, Embase, Biosis, Caplus, PCTfull

google

Terms searched: EGF domain, EGF repeat, cysteine-rich domain, EGF, Neuregulin, Heregulin, splicing, NGR